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Binase Immobilized on halloysite nanotubes exerts enhanced cytotoxicity toward human colon adenocarcinoma cells

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Abstract

© 2017 Khodzhaeva, Makeeva, Ulyanova. Many ribonucleases (RNases) are considered as promising tools for antitumor therapy because of their selective cytotoxicity toward cancer cells. Binase, the RNase from Bacillus pumilus, triggers apoptotic response in cancer cells expressing RAS oncogene which is mutated in a large percentage of prevalent and deadly malignancies including colorectal cancer. The specific antitumor effect of binase toward RAS-transformed cells is due to its direct binding of RAS protein and inhibition of downstream signaling. However, the delivery of proteins to the intestine is complicated by their degradation in the digestive tract and subsequent loss of therapeutic activity. Therefore, the search of new systems for effective delivery of therapeutic proteins is an actual task. This study is aimed to the investigation of antitumor effect of binase immobilized on natural halloysite nanotubes (HNTs). Here, we have developed the method of binase immobilization on HNTs and optimized the conditions for the enzyme loading and release (i); we have found the non-toxic concentration of pure HNTs which allows to distinguish HNTs- and binase-induced cytotoxic effects (ii); using dark-field and fluorescent microscopy we have proved the absorption of binase-loaded HNTs on the cell surface (iii) and demonstrated that binase-halloysite nanoformulations possessed twice enhanced cytotoxicity toward tumor colon cells as compared to the cytotoxicity of binase itself (iv). The enhanced antitumor activity of biocompatible binase-HNTs complex confirms the advisability of its future development for clinical practice.

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Keywords

Bacillus pumilus, Binase, Colon adenocarcinoma, Cytotoxicity, Halloysite, Nanotubes, RNase

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